

II. REMARKS/ARGUMENTS

A. Regarding the Amendments

Claims 23-39 are pending. Claims 23-33 were originally submitted at the filing of the subject application. Claims 34-39 are newly added.

Claims 34-37 recite specific types of neoplastic growth. Support can be found, *inter alia*, at page 9, lines 1-4 and Example 2 in the specification. No new matter is added by the amendments. Entering of the amendments is respectfully requested.

B. Rejection under 35 U.S.C. §112, first paragraph

Claims 23-33 are rejected as the full scope of the claims are allegedly not being enabled. Applicant respectfully traverses this rejection.

The Office Action states that the specification enables the treatment of neoplastic growth in breast cancer, however does not reasonably provide enablement for the treatment of other neoplastic growth. Applicant respectfully submits that the specification teaches how to make and use the full scope of the present invention, thus one skilled in the art is enabled to use the present invention for the treatment of various neoplastic growth.

Specifically, the specification teaches that the indolocarbazole derivatives in combination with radiation can be used to treat any neoplastic growth, *e.g.*, various abnormal growth in tumor or cancer cells. The specification also lists several examples of neoplastic growth including prostate cancer, bone tumor, colon cancer, lymphoma, and brain tumor. (See page 9, lines 1-4 in the specification.). In addition, the specification provides examples to demonstrate the efficacy of the present invention in different types of cells including Chinese hamster ovarian CHO cells and human breast cancer MCF-7 cells. (See Example 2 at pages 15-16 in the specification.).

The specification also teaches the dosage, pharmaceutical carrier, duration of treatment and route of administration of the indolocarbazole derivatives in association with radiation or radiation with an anti-neoplastic chemotherapeutic agent. For example, the specification teaches that indolocarbazole derivatives can be used at a non-cytotoxic level or radiosensitivity increasing amount such as at least 1, 2, 5, or 10 µg/ml to treat neoplastic growth (page 9, lines 5-

9 and page 10, lines 1-5 in the specification). Examples are also provided to illustrate the use of indolocarbazole derivatives at 2 µg/ml and 10 µg/ml in Chinese hamster ovarian CHO cells and at 2 µg/ml in human breast cancer MCF-7 cells (Example 2 at pages 15 and 16 in the specification).

The specification also teaches that any suitable pharmaceutical carrier can be used with the indolocarbazole derivatives of the present invention, which are usually prepared as injectables, either as liquid or suspension, or solid forms suitable for solution or suspension in liquid vehicles prior to injection. (See pages 9 and 10 in the specification.). Contrary to the Office Action's assertion that "there do not appear to be any examples or teachings in the prior art wherein a structure similar to the claimed structure was administered to a subject to treat development of any neoplastic growth", indolocarbazole derivatives belong to a class of known DNA topoisomerase I-targeted cancer drugs; and one skilled in the art is familiar with using this class of compounds in treating neoplastic growth. See page 2, lines 15-31 and page 3 lines 1-2 in the specification.

To the extent that the enablement rejection is in fact based on skepticism about the invention, Applicant points out that the statements of generic operability in the specification must be accepted as accurate in the absence of proof to the contrary. Wettstein v. Campbell 139, USPQ 341, 343 (BOPI 1962). Thus, whenever a rejection is based on the contention that the disclosure is not commensurate in scope with the subject matter being claimed, "it is incumbent upon the Patent and Trademark Office....to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement (emphasis added)." In re Marzocchi 169 USPQ 367, 369-370 (CCPA 1971).

In the present case, the Office Action has clearly failed to provide any evidence or sound reasoning in support of its contention that the full scope of the claims are not enabled. For example, the Office Action has failed to provide any evidence showing that one skilled in the art would think the teaching in the present invention is incredible, especially any evidence showing one skilled in the art would doubt that the present invention could be used to treat various neoplastic growth.

In addition, the Office Action has failed to provide any evidence to support its own skepticism about the teaching of the present invention. In particular, the Office Action has failed to show why neoplastic growth in breast cancer is different from other neoplastic growth and why the present invention when used as taught in the specification will not be operable in treating other neoplastic growth in addition to the neoplastic growth in breast cancer.

It has long been held by the Court of Appeals for the Federal Circuit and its predecessor that a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. In re Brana, 34 USPQ2d 1437, 1441 (Fed. Cir. 1995) citing In re Marzocchi, 169 USPQ 367, 369 (CCPA, 1971).

Therefore, the present invention is fully enabled since the specification teaches how to make and use indolocarbazole derivatives in treating various neoplastic growth and the Office Action has failed to provide any evidence to support its position that the present invention would not be operable in treatment of neoplastic growth other than breast cancer. Withdrawal of the rejection is respectfully requested.

C. Rejections under 35 U.S.C. §103(a)

Claims 23-33 are rejected as being obvious over Chen et al. (1997) in view of Prudhomme (2000). These rejections are respectfully traversed.

Chen et al disclose that an intact stereospecific interaction between camptothecin derivatives and DNA topoisomerase I is essential in the induction of radiosensitization. Prudhomme discloses that analogues of the bacterial metabolite rebeccamycin belong to a new family of topoisomerase I inhibitors. The Office Action suggests that based on the prior art disclosure one skilled in the art would have replaced camptothecin with rebeccamycin analogues and expected the same effect in induction of radiosensitization.

Applicant respectfully points out that although camptothecin derivatives and rebeccamycin analogues are both DNA topoisomerase I targeted drugs (which are defined based

on their cytotoxicity, but not on their radiosensitizing activity), they are structurally very different and belong to different classes of chemical compounds. One skilled in the art usually substitute compounds based on their chemical or structural similarities, but not the target or binding partner of the compounds, *e.g.*, one skilled in the art would not have believed that camptothecin could be replaced by rebeccamycin analogues because they are involved in the same target. In other words, just because camptothecin derivatives are DNA topoisomerase I targeted drugs and can induce radiosensitization, it does not necessary mean that all DNA topoisomerase I targeted drugs can induce radiosensitization. The mechanism of radiosensitization induced by camptothecin derivatives and indolocarbazole derivatives remains largely unknown and could be totally different. It is conceivable that each class of DNA topoisomerase I targeted compounds interact with DNA topoisomerase I in their unique way, and only some but not all such interaction may be related to radiosensitization.

Furthermore, even within the same generic class not every subclass or compound is necessarily capable of the same function. Examples provided by the present invention specifically demonstrate that although indolocarbazole derivatives are generally considered DNA topoisomerase I targeted drugs, not all subclasses of indolocarbazole derivatives can induce radiosensitization. Some subclasses of indolocarbazole derivatives are potent inducers of topoisomerase I- mediated DNA damage and cytotoxicity, however they fail to have any significant effect in inducing radiosensitization. See Examples 2 and 6 in the specification. Such result specifically undermines the presumption relied upon by the Office Action and illustrates that only certain, but not all, topoisomerase I targeted drugs are capable of inducing radiosensitization.

In summary, the disclosure of the cited prior art would not have made it obvious for one skilled in the art to replace camptothecin with rebeccamycin analogues and reasonably expect the same effect in induction of radiosensitization. Furthermore, the cited prior art does not teach or suggest the radiosensitizing function of the specific subclasses of indolocarbazole derivatives used in the present invention. Therefore, the Office Action has failed to make a *prima facie* case to show why the present invention is obvious over the cited prior art. Withdrawal of the rejection is respectfully requested.

Appl. No. 10/075,718
Amdt. dated January 21, 2004
Reply to Office Action of October 21, 2003

In view of the amendment and the above remarks, it is submitted that the claims are in condition for allowance and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Dated: 1/20/04

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